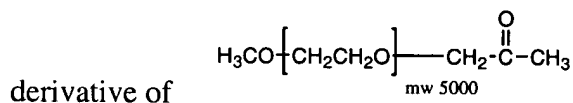
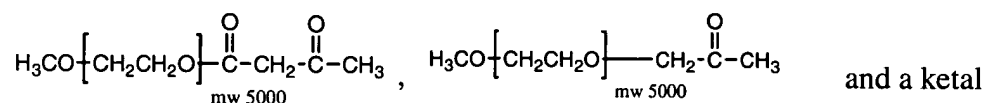


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What is claimed is:

1. A polymeric reagent comprising a functional group and water-soluble polymer segment having a weight average molecular weight of greater than 2,200, wherein the functional group is attached to the water-soluble polymer segment through either a direct covalent bond or through one or more atoms, and further wherein (a) the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal, and (b) the polymeric reagent lacks each of the following: an aromatic moiety; a residue of proline; a cyclic dienone, a saturated hydrocarbon chain of 8 carbons or greater; and a -ONH<sub>2</sub> group, with the proviso that the polymeric reagent is none of



2. The polymeric reagent of claim 1, wherein the water-soluble polymer segment is a poly(ethylene glycol).

3. The polymeric reagent of claim 2, wherein the poly(ethylene glycol) is terminally capped with an end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.

4. The polymeric reagent of claim 2, wherein the poly(ethylene glycol) is terminally capped with methoxy.

5. The polymeric reagent of claim 2, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 2,500 Daltons to about 100,000 Daltons.

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6. The polymeric reagent of claim 5, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 4,900 Daltons to about 40,000 Daltons.

7. The polymeric reagent of claim 6, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 9,900 Daltons to about 25,000 Daltons.

8. The polymeric reagent of claim 2, wherein the functional group is a ketone.

9. The polymeric reagent of claim 2, wherein the functional group is a ketone hydrate.

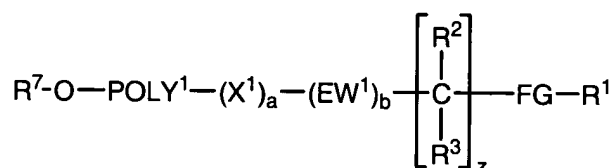
10. The polymeric reagent of claim 2, wherein the functional group is a hemiketal.

11. The polymeric reagent of claim 2, wherein the functional group is a ketal.

12. The polymeric reagent of claim 2, lacking any halogen atoms.

13. The polymeric reagent of claim 2, wherein a methyl group is alpha or beta to the functional group.

14. A polymeric reagent comprising the following structure:



wherein:

POLY<sup>1</sup> is a water-soluble polymer segment having a terminus defined as -O-R<sup>7</sup>;

(a) is either zero or one;

(b) is either zero or one;

X<sup>1</sup>, when present, is a spacer moiety;

EW<sup>1</sup>, when present, is an electron-withdrawing group;

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(z) is an integer from 2 to 7;

each occurrence of  $R^2$  is independently H or a nonaromatic-containing organic radical;

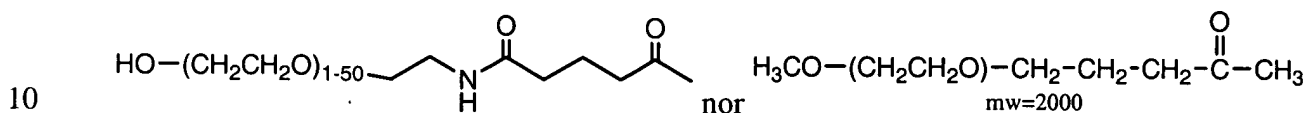
each occurrence of  $R^3$  is independently H or a nonaromatic-containing organic radical;

$R^7$  is H or a nonaromatic-containing organic radical;

5 FG is a functional group selected from ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal; and

$R^1$  is a nonaromatic-containing organic radical;

and further wherein the  $\left[ \begin{array}{c} R^2 \\ | \\ -C- \\ | \\ R^3 \end{array} \right]_z$  moiety optionally contains one or more double bonds,  
with the proviso that the polymeric reagent is neither



15 15. The polymeric reagent of claim 14, wherein the water-soluble polymer segment ("POLY<sup>1</sup>") is a poly(ethylene glycol).

15 16. The polymeric reagent of claim 15, wherein the poly(ethylene glycol) is  $-\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_m-\text{OCH}_2\text{CH}_2-$ , wherein (m) is from about 55 to about 3,000.

20 17. The polymeric reagent of claim 15, wherein  $R^7$  is a nonaromatic-containing organic radical comprising nine or less carbon atoms.

18. The polymeric reagent of claim 15, wherein  $R^7$  is H or methyl.

19. The polymeric reagent of claim 15, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 2,500 Daltons to about 100,000 Daltons.

25 20. The polymeric reagent of claim 19, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 4,900 Daltons to about 40,000 Daltons.

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21. The polymeric reagent of claim 20, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 9,900 Daltons to about 25,000 Daltons.

22. The polymeric reagent of claim 15, wherein the functional group is a ketone.

23. The polymeric reagent of claim 15, wherein the functional group is a ketone hydrate.

24. The polymeric reagent of claim 15, wherein the functional group is a hemiketal.

25. The polymeric reagent of claim 15, wherein the functional group is a ketal.

26. The polymeric reagent of claim 15, wherein the functional group is selected from the group consisting of thione, monothiohydrate, dithiohydrate, monothiohemiketal, dithiohemiketal, and dithioketal.

27. The polymeric reagent of claim 15, lacking halogen atoms.

28. The polymeric reagent of claim 15, wherein each occurrence of  $R^2$  and  $R^3$  is H.

29. The polymeric reagent of claim 16, wherein the  $R^2$  attached to the carbon  $\alpha$  to FG is alkyl, all other  $R^2$  are H, and each occurrence of  $R^3$  is H.

30. The polymeric reagent of claim 15, wherein (a) is one and  $X^1$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -O-C(O)-NH-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,

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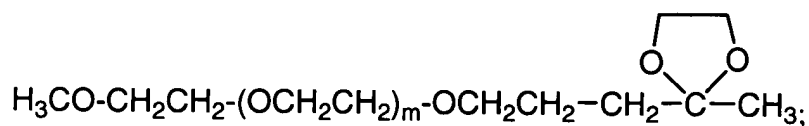
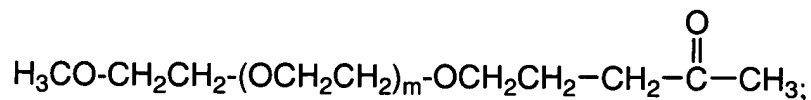
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 10 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -O-C(O)-NH-[CH<sub>2</sub>]<sub>0-6</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>0-2</sub>-, -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-,  
 -NH-C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-, -O-C(O)-CH<sub>2</sub>-, -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, and  
 15 -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-.

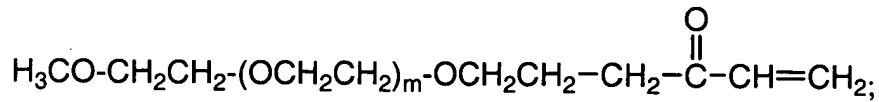
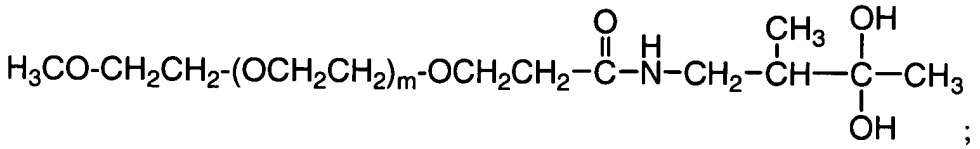
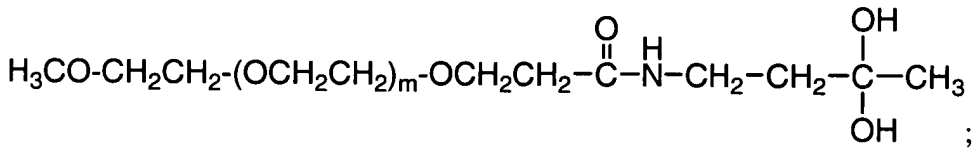
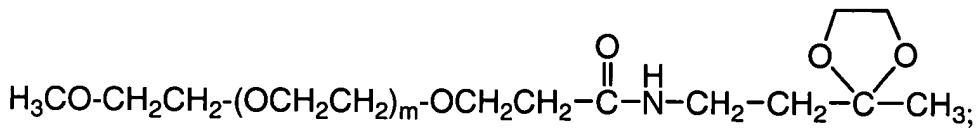
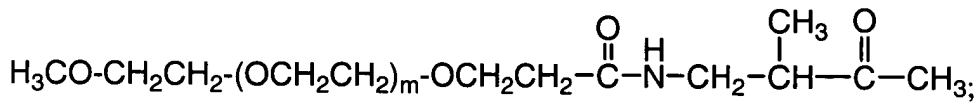
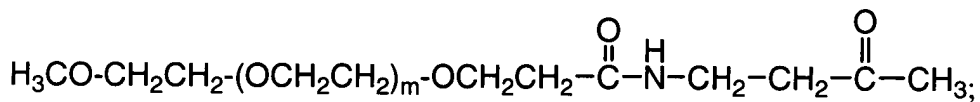
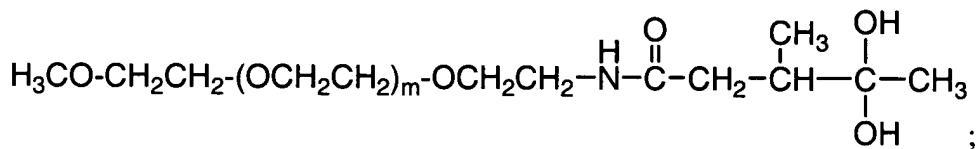
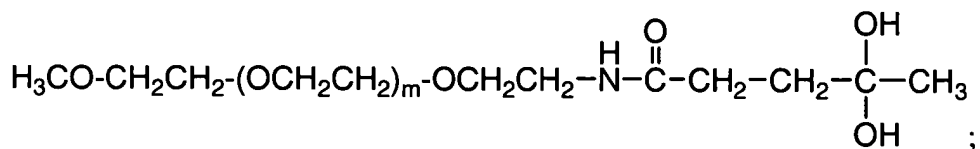
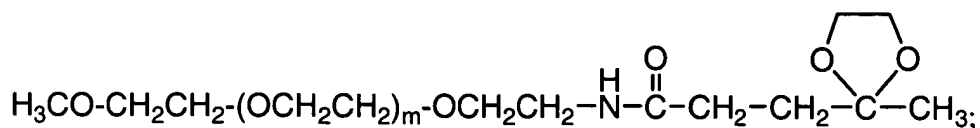
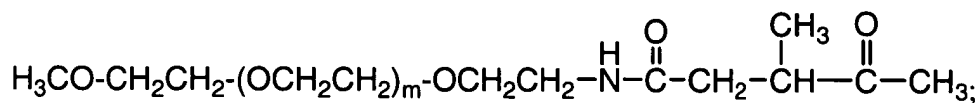
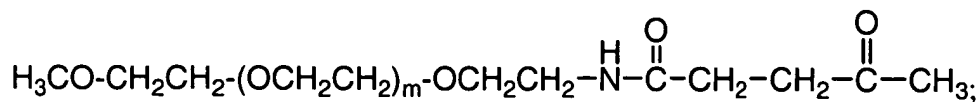
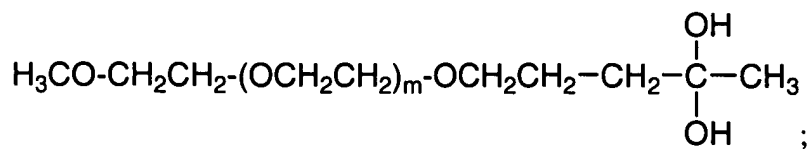
31. The polymeric reagent of claim 15, wherein (b) is one and EW<sup>1</sup> is selected from the  
 group consisting of -O-, -NH-, -NHC(O)-, -C(O)NH-, -OC(O)-, -OC(O)-, -OC(O)-NH-,  
 -NH-OC(O)-, -C(O)-, -C(S)-, and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent.

32. The polymeric reagent of claim 15, wherein R<sup>1</sup> is methyl.

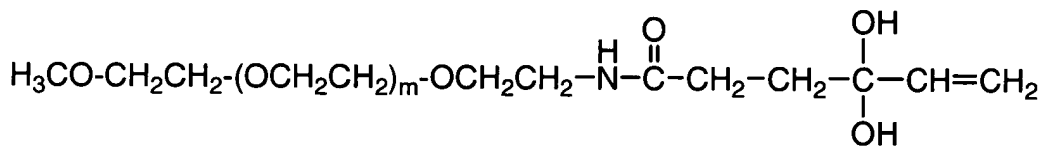
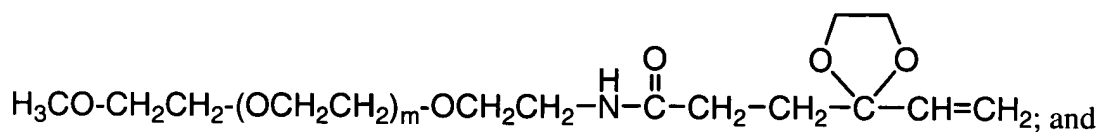
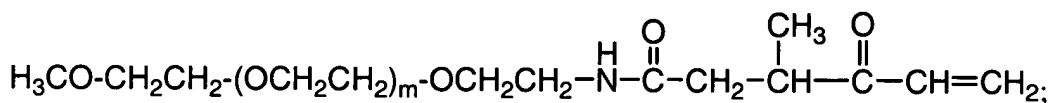
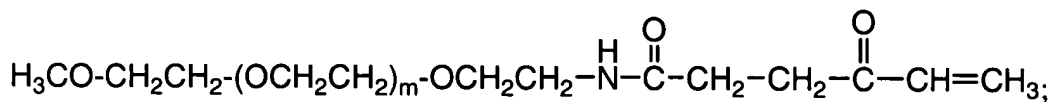
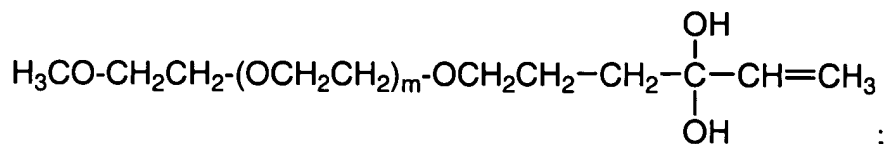
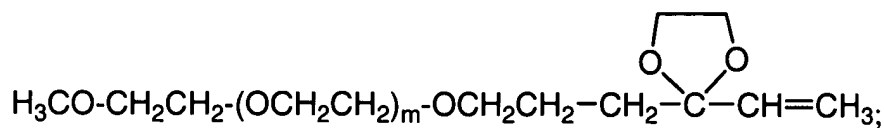
33. The polymeric reagent of claim 15, wherein R<sup>1</sup> is -CH=CH<sub>2</sub>.

34. The polymeric reagent of claim 15, selected from the group consisting of:





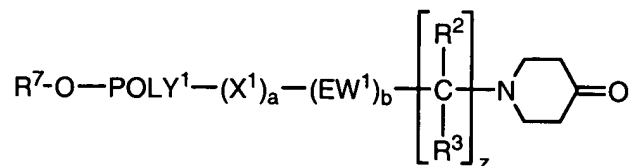
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wherein (m) is from about 3 to about 3000.

35. A polymeric reagent comprising water-soluble polymer segment and a functional group, wherein the functional group is part of a cyclic structure and further wherein the cyclic structure is attached to the water-soluble polymer segment through either a direct covalent bond or through one or more atoms, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal, and further wherein the polymeric reagent lacks a cyclic dienone.

36. The polymeric reagent of claim 35, comprising the following structure:



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wherein:

POLY<sup>1</sup> is a water-soluble polymer segment having a terminus defined as -O-R<sup>7</sup>;

(a) is either zero or one;

(b) is either zero or one;

X<sup>1</sup>, when present, is a spacer moiety;

EW<sup>1</sup>, when present, is an electron-withdrawing group;

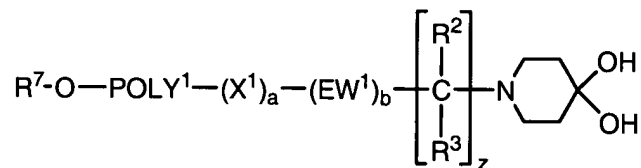
(z) is zero or a positive an integer;

each occurrence of R<sup>2</sup>, when present, is independently H or an organic radical;

each occurrence R<sup>3</sup>, when present, is independently H or an organic radical; and

R<sup>7</sup> is H or an organic radical.

37. The polymeric reagent of claim 35, comprising the following structure:



wherein:

POLY<sup>1</sup> is a water-soluble polymer segment having a terminus defined as -O-R<sup>7</sup>;

(a) is either zero or one;

(b) is either zero or one;

X<sup>1</sup>, when present, is a spacer moiety;

EW<sup>1</sup>, when present, is an electron-withdrawing group;

(z) is zero or a positive an integer;

each occurrence of R<sup>2</sup>, when present, is independently H or an organic radical;

each occurrence R<sup>3</sup>, when present, is independently H or an organic radical; and

R<sup>7</sup> is H or an organic radical.

38. The polymeric reagent of claims 36 or 37, wherein the water-soluble polymer segment ("POLY") is a poly(ethylene glycol).



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39. The polymeric reagent of claim 35, wherein the poly(ethylene glycol) is  $-\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_m-\text{OCH}_2\text{CH}_2-$ , wherein (m) is from about 3 to about 3,000.

40. The polymeric reagent of claim 38, wherein the poly(ethylene glycol) is branched.

41. The polymeric reagent of claims 36 or 37, wherein  $\text{R}^7$  is a nonaromatic organic radical comprising nine or less carbon atoms.

42. The polymeric reagent of claims 36 or 37, wherein  $\text{R}^7$  is H or methyl.

43. The polymeric reagent of claim 38, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 2,500 Daltons to about 100,000 Daltons.

44. The polymeric reagent of claim 43, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 4,900 Daltons to about 40,000 Daltons.

45. The polymeric reagent of claim 44, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 9,900 Daltons to about 25,000 Daltons.

46. The polymeric reagent of claim 35, wherein the functional group is selected from the group consisting of thione, monothiohydrate, dithiohydrate, monothiohemiketal, dithiohemiketal, and dithiohemiketal.

47. The polymeric reagent of claim 35, lacking halogen atoms.

48. The polymeric reagent of claims 36 or 37, lacking an aromatic moiety.

49. The polymeric reagent of claims 36 or 37, lacking an enone.

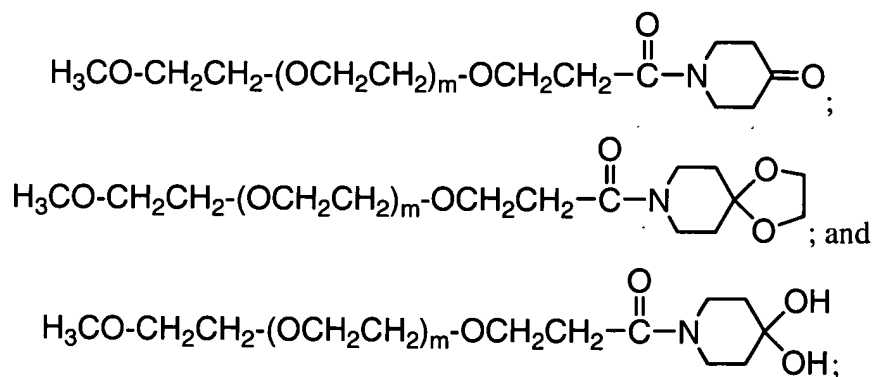
50. The polymeric reagent of claims 36 or 37, wherein (z) is zero, (b) is one, and  $\text{EW}^1$  is selected from the group consisting of  $-\text{O}-$ ,  $-\text{NH}-$ ,  $-\text{NHC}(\text{O})-$ ,  $-\text{C}(\text{O})\text{NH}-$ ,  $-\text{OC}(\text{O})-$ ,  $-\text{OC}(\text{O})-$ ,

-OC(O)-NH-, -NH-OC(O)-, -C(O)-, -C(S)-, and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent.

51. The polymeric reagent of claim 50, wherein EW<sup>1</sup> is -C(O)-.

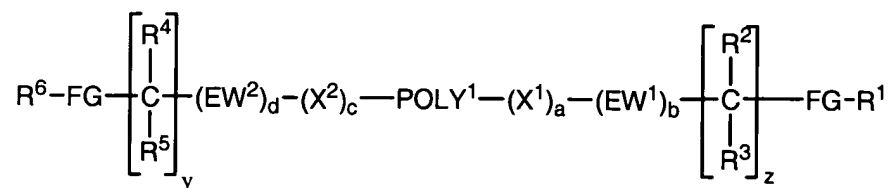
52. The polymeric reagent of claim 35, wherein the cyclic structure is selected from the group consisting of piperidiny, cyclohexyl, cyclopentyl, bicyclo[2,2,1]heptanyl, bicyclo[2,2,1]hexanyl, bicyclo[3,2,1]octanyl, bicyclo[3,1,1]heptanyl, bicyclo[3,3,1]nonanyl, cyclobutyl, cycloheptyl, cyclooctyl, oxa and aza forms thereof, and dioxo and diaza forms of any of the foregoing.

53. The polymeric reagent of claim 35, selected from the group consisting of:



wherein (m) is from about 3 to about 3000, (a) is zero or one, (e) is zero or one, X<sup>1</sup> is a spacer moiety when present, and X<sup>3</sup> is a spacer moiety when present.

54. A polymeric reagent comprising the following structure:



wherein:

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POLY<sup>1</sup> is a water-soluble polymer segment having a molecular weight of greater than 2,200 Daltons;

(a) is either zero or one;

(b) is either zero or one;

5 (c) is either zero or one;

(d) is either zero or one;

X<sup>1</sup>, when present, is a spacer moiety;

X<sup>2</sup>, when present is a spacer moiety;

EW<sup>1</sup>, when present, is an electron-withdrawing group;

10 EW<sup>2</sup>, when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

(y) is zero or a positive integer from 1 to 7;

each occurrence of R<sup>2</sup> is independently H or an organic radical;

each occurrence of R<sup>3</sup> is independently H or an organic radical;

15 each occurrence of R<sup>4</sup> is independently H or an organic radical;

each occurrence of R<sup>5</sup> is independently H or an organic radical;

FG-R<sup>1</sup> is either (i) a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal having a terminus defined as R<sup>1</sup>, wherein R<sup>1</sup> is an organic radical, or (ii) a nondienone cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure; and

20 FG-R<sup>6</sup> is either (i) a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal having a terminus defined as R<sup>6</sup>, wherein R<sup>6</sup> is an organic radical, or (ii) a nondienone cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure.

30 55. The polymeric reagent of claim 54, wherein the water-soluble polymer segment ("POLY<sup>1</sup>") is a poly(ethylene glycol).

56. The polymeric reagent of claim 55, wherein the poly(ethylene glycol) is  $-\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_m-\text{OCH}_2\text{CH}_2-$ , wherein (m) is from about 55 to about 3,000.

5 57. The polymeric reagent of claim 55, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 2,500 Daltons to about 100,000 Daltons.

58. The polymeric reagent of claim 57, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 4,900 Daltons to about 40,000 Daltons.

10 59. The polymeric reagent of claim 58, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 9,900 Daltons to about 25,000 Daltons.

15 60. The polymeric reagent of claim 55, wherein each functional group of  $\text{FG-R}^1$  and  $\text{FG-R}^6$  is a ketone.

61. The polymeric reagent of claim 55, wherein each functional group of  $\text{FG-R}^1$  and  $\text{FG-R}^6$  is a ketone hydrate.

20 62. The polymeric reagent of claim 55, wherein each functional group of  $\text{FG-R}^1$  and  $\text{FG-R}^6$  is a hemiketal.

63. The polymeric reagent of claim 55, wherein each functional group of  $\text{FG-R}^1$  and  $\text{FG-R}^6$  is a ketal.

25 64. The polymeric reagent of claim 55, wherein each functional group of  $\text{FG-R}^1$  and  $\text{FG-R}^6$  selected from the group consisting of thione, monothiohydrate, dithiohydrate, monothiohemiketal, and dithioketal.

30 65. The polymeric reagent of claim 55, lacking halogen atoms.

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66. The polymeric reagent of claim 55, lacking an aromatic moiety.

67. The polymeric reagent of claim 55, wherein each of (y) and (z) is a positive integer from 1 to 7, and each occurrence of  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  is H.

5

68. The polymeric reagent of claim 55, wherein each of (y) and (z) is a positive integer from 2 to 7.

69. The polymeric reagent of claim 55, wherein each of (y) and (z) is a positive integer from 1 to 7,  $R^2$  attached to the carbon  $\alpha$  to  $FG-R^1$  is alkyl,  $R^4$  attached to the carbon  $\alpha$  to  $-FG-R^6$  is alkyl, all other  $R^2$  and  $R^4$ , when present, are H, and each occurrence of  $R^3$  and  $R^5$  is H.

10

70. The polymeric reagent of claim 55, wherein each of  $FG-R^1$  and  $FG-R^6$  is a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal having a terminus defined as  $R^1$ , wherein  $R^1$  is an organic radical selected from methyl and  $-CH=CH_2$ .

15

71. The polymeric reagent of claim 55, each of  $FG-R^1$  and  $FG-R^6$  is a nondienone cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure and further wherein the cyclic structure is selected from the group consisting of piperidinyl, cyclohexyl, cyclopentyl, bicyclo[2,2,1]heptanyl, bicyclo[2,2,1]hexanyl, bicyclo[3,2,1]octanyl, bicyclo[3,1,1]heptanyl, bicyclo[3,3,1]nonanyl, cyclobutyl, cycloheptyl, cyclooctyl, oxa and aza forms thereof, and dioxo and diaza forms of any of the foregoing.

20

25

72. The polymeric reagent of claim 55, wherein (b) and (d) are each one and  $EW^1$  is selected from the group consisting of  $-O-$ ,  $-NH-$ ,  $-NHC(O)-$ ,  $-C(O)NH-$ ,  $-OC(O)-$ ,  $-OC(O)-$ ,  $-OC(O)-NH-$ ,  $-NH-OC(O)-$ ,  $-C(O)-$ ,  $-C(S)-$ , and  $-C(OR)H-$ , wherein OR is an alkoxy or hydroxy substituent and  $EW^2$  is selected from the group consisting of  $-O-$ ,  $-NH-$ ,  $-C(O)NH-$ ,  $-NHC(O)-$ ,

30

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-OC(O)-, -OC(O)-, -NH-OC(O)-, -OC(O)-NH-, -C(O)-C(S)- and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent.

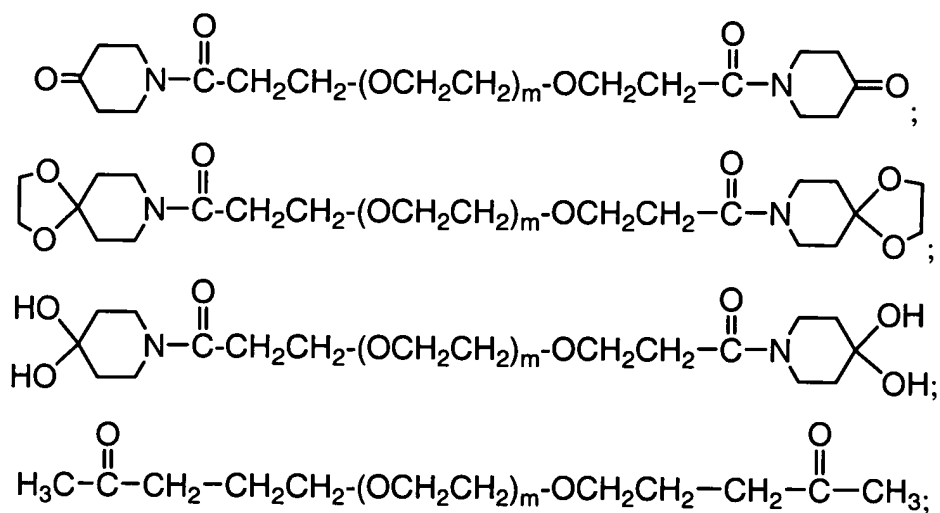
73. The polymeric reagent of claim 55, wherein each of (a) and (c) is one,  $X^1$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -O-C(O)-NH-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -C(O)-O-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-[CH<sub>2</sub>]<sub>0.6</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>0.2</sub>-, -C(O)-NH-(CH<sub>2</sub>)<sub>1.6</sub>-NH-C(O)-, -NH-C(O)-NH-(CH<sub>2</sub>)<sub>1.6</sub>-NH-C(O)-, -O-C(O)-CH<sub>2</sub>-, -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, and -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, and  $X^2$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -NH-C(O)-O-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-,

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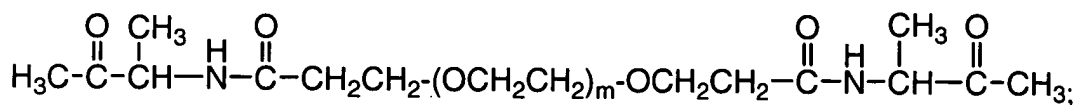
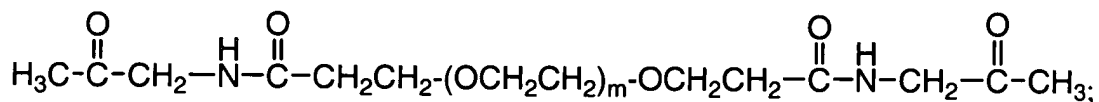
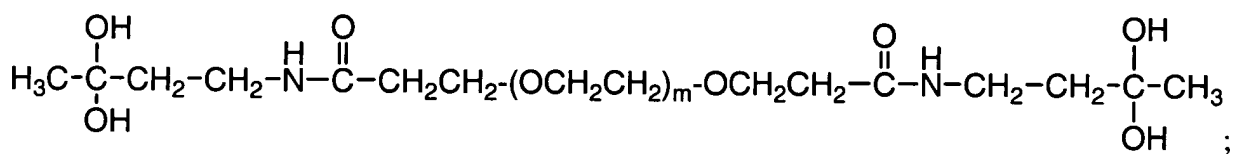
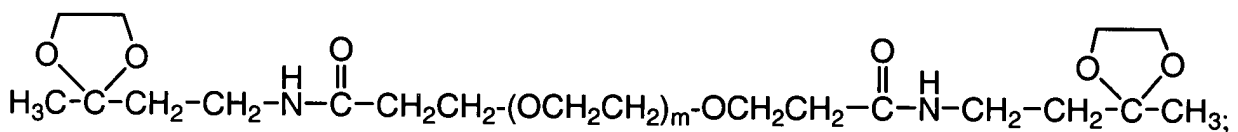
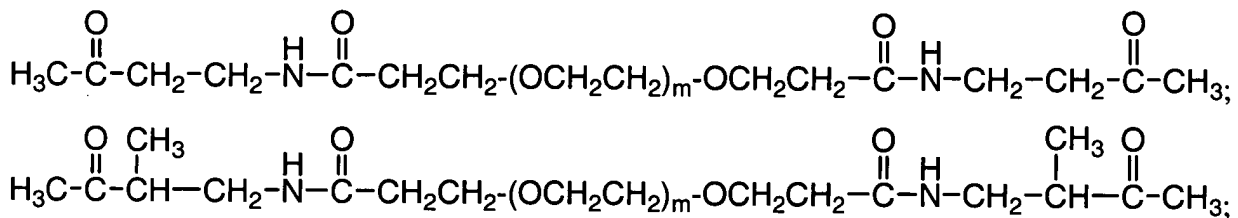
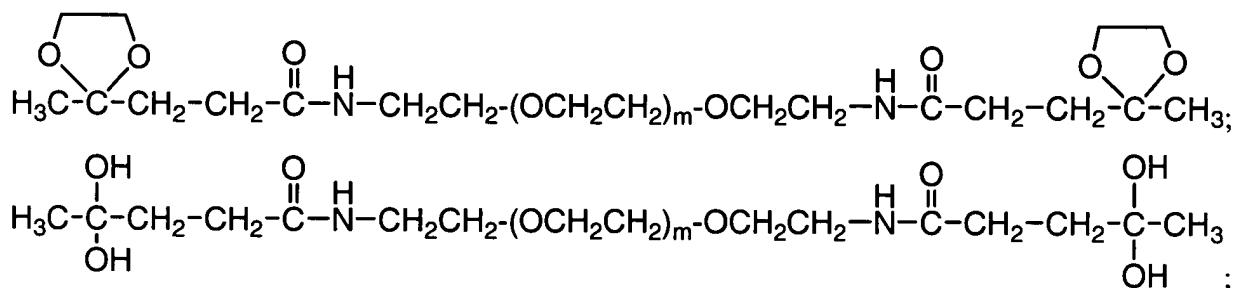
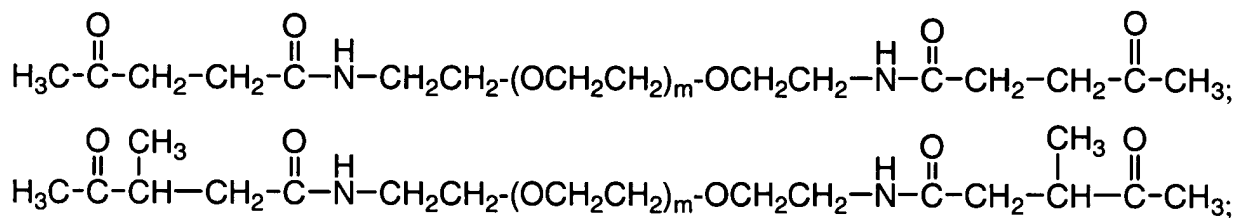
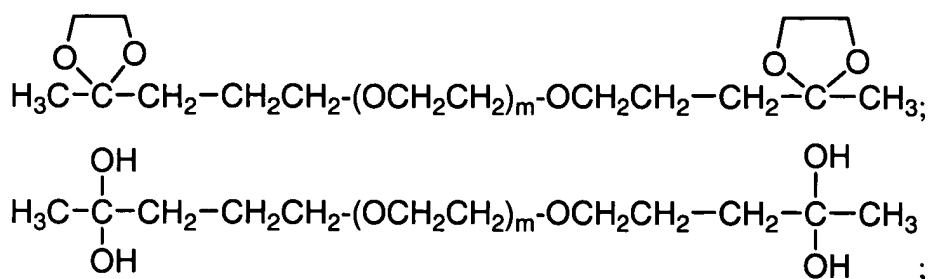
- CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-,  
 5 -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C(O)-,  
 -CH<sub>2</sub>-O-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-C(O)-, -CH<sub>2</sub>-C(O)-NH-,  
 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-,  
 10 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-O-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-O-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-O-, -CH<sub>2</sub>-NH-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 15 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>0.2</sub>-(CH<sub>2</sub>)<sub>0.6</sub>-NH-C(O)-O-, -C(O)-NH-(CH<sub>2</sub>)<sub>1.6</sub>-NH-C(O)-,  
 -C(O)-NH-(CH<sub>2</sub>)<sub>1.6</sub>-NH-C(O)-NH-, -CH<sub>2</sub>-C(O)-O-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-, and  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-.

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74. The polymeric reagent of claim 54, selected from the group consisting of:

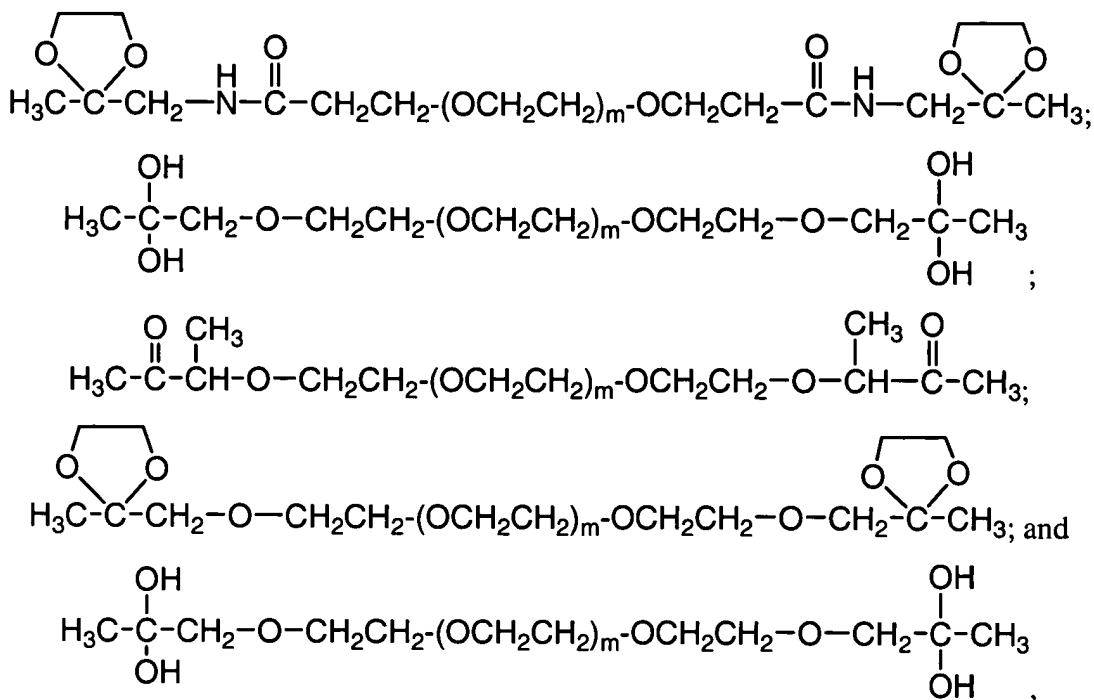


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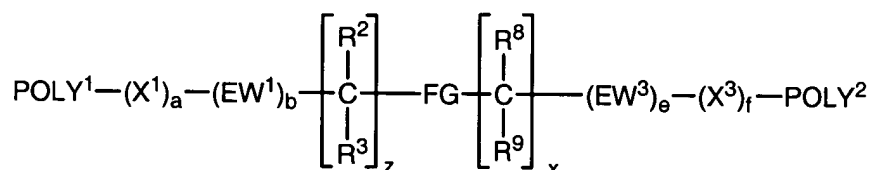
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wherein (m) is from about 55 to about 3000.

75. A polymeric reagent comprising a first water-soluble polymer segment, a first water-soluble polymer segment, a second water-soluble polymer segment, and a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal, wherein each of the first and second water-soluble polymer segments are attached, either through a direct covalent bond or through one or more atoms, to the functional group and further wherein when the functional group is a ketone, ketone hydrate, hemiketal or ketal: (a) the polymeric reagent lacks an aromatic moiety; or (b) each water-soluble polymer segment in the polymeric reagent has a weight average molecule weight of 1000 Daltons or greater.

76. The polymeric reagent of claim 75, comprising the following structure:



wherein:

POLY<sup>1</sup> is the first water-soluble polymer segment;

POLY<sup>2</sup> is the second water-soluble polymer segment;

(a) is either zero or one;

(b) is either zero or one;

(e) is either zero or one;

(f) is either zero or one;

X<sup>1</sup>, when present, is a spacer moiety;

X<sup>3</sup>, when present is a spacer moiety;

EW<sup>1</sup>, when present, is an electron-withdrawing group;

EW<sup>3</sup>, when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

(x) is zero or a positive integer from 1 to 7;

each occurrence of R<sup>2</sup>, when present, is independently H or an organic radical;

each occurrence of R<sup>3</sup>, when present, is independently H or an organic radical;

each occurrence of R<sup>8</sup>, when present, is independently H or an organic radical;

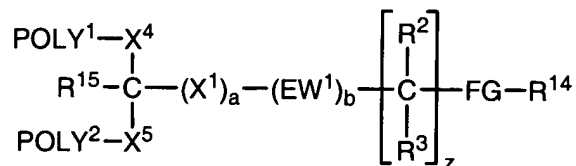
each occurrence of R<sup>9</sup>, when present, is independently H or an organic radical; and

FG is the functional group selected from ketone, ketone hydrate, thione,

monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and

dithioketal.

77. The polymeric reagent of claim 75, comprising the following structure:



wherein:

POLY<sup>1</sup> is the first water-soluble polymer segment;

POLY<sup>2</sup> is the second water-soluble polymer segment;

(a) is either zero or one;

(b) is either zero or one;

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$X^1$ , when present, is a spacer moiety;

$X^4$  is a spacer moiety;

$X^5$  is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

each occurrence of  $R^2$ , when present, is independently H or an organic radical;

each occurrence of  $R^3$ , when present, is independently H or an organic radical;

$R^{15}$  is H or a noninterfering organic radical; and

$FG-R^{14}$  is either (i) a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal having a terminus defined as  $R^{14}$ , wherein  $R^{14}$  is an organic radical, or (ii) a cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure.

78. The polymeric reagent of claims 65 or 66, wherein each water-soluble polymer segment ("POLY<sup>1</sup>" and "POLY<sup>2</sup>") is a poly(ethylene glycol).

79. The polymeric reagent of claim 78, wherein each poly(ethylene glycol) is  $-CH_2CH_2-(OCH_2CH_2)_m-OCH_2CH_2-$ , wherein (m) is from about 25 to about 3,000.

80. The polymeric reagent of claim 78, wherein each poly(ethylene glycol) is terminally capped with an end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.

81. The polymeric reagent of claim 78, wherein each poly(ethylene glycol) is terminally endcapped with an alkoxy.

82. The polymeric reagent of claim 78, wherein each poly(ethylene glycol) is terminally endcapped with methoxy.

83. The polymeric reagent of claim 78, wherein each poly(ethylene glycol) is terminally endcapped with hydroxy.

5        84. The polymeric reagent of claim 78, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 2,500 Daltons to about 100,000 Daltons.

85. The polymeric reagent of claim 84, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 4,900 Daltons to about 40,000 Daltons.

10       86. The polymeric reagent of claim 85, wherein the poly(ethylene glycol) has a nominal average molecular weight of from about 9,900 Daltons to about 25,000 Daltons.

87. The polymeric reagent of claim 78, lacking halogen atoms.

15       88. The polymeric reagent of claim 78, lacking an aromatic moiety.

89. The polymeric reagent of claim 76, wherein each of (x) and (z) is a positive integer from 1 to 7, and each occurrence of  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  is H.

20       90. The polymeric reagent of claim 76, wherein each of (x) and (z) is a positive integer from 2 to 7.

25       91. The polymeric reagent of claim 76, wherein (b) and (e) are each one and  $EW^1$  is selected from the group consisting of -O-, -NH-, -NHC(O)-, -C(O)NH-, -OC(O)-, -OC(O)-, -OC(O)-NH-, -NH-OC(O)-, -C(O)-, -C(S)-, and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent, and  $EW^2$  is selected from the group consisting of -O-, -NH-, -C(O)NH-, -NHC(O)-, -OC(O)-, -OC(O)-, -NH-OC(O)-, -OC(O)-NH-, -C(O)-C(S)- and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent.

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92. The polymeric reagent of claim 76, wherein each of (a) and (f) is one,  $X^1$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -O-C(O)-NH-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -C(O)-O-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-[CH<sub>2</sub>]<sub>0-6</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>0-2</sub>-, -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-, -NH-C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-, -O-C(O)-CH<sub>2</sub>-, -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, and -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, and  $X^3$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -NH-C(O)-O-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,

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$\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-}$ ,  
 $\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-O-C(O)-}$ ,  
 $\text{-CH}_2\text{-O-C(O)-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-O-C(O)-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-O-C(O)-}$ ,  $\text{-CH}_2\text{-C(O)-NH-}$ ,  
5  $\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-C(O)-NH-}$ ,  
 $\text{-CH}_2\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-C(O)-NH-CH}_2\text{-}$ ,  
 $\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-NH-C(O)-O-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-O-}$ ,  
 $\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(O)-O-}$ ,  $\text{-CH}_2\text{-NH-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-NH-}$ ,  $\text{-CH}_2\text{-NH-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-NH-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-CH}_2\text{-C(O)-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-C(O)-}$ ,  $\text{-CH}_2\text{-C(O)-CH}_2\text{-}$ ,  $\text{-CH}_2\text{-C(O)-CH}_2\text{-CH}_2\text{-}$ ,  
10  $\text{-CH}_2\text{-CH}_2\text{-C(O)-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-C(O)-CH}_2\text{-CH}_2\text{-}$ ,  $\text{-NH-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-CH}_2\text{-CH}_2\text{-C(O)-NH-CH}_2\text{-CH}_2\text{-NH-C(O)-CH}_2\text{-CH}_2\text{-CH}_2\text{-}$ ,  
 $\text{-(CH}_2\text{CH}_2\text{O)}_{0.2}\text{-(CH}_2\text{)}_{0.6}\text{-NH-C(O)-O-}$ ,  $\text{-C(O)-NH-(CH}_2\text{)}_{1.6}\text{-NH-C(O)-}$ ,  
15  $\text{-C(O)-NH-(CH}_2\text{)}_{1.6}\text{-NH-C(O)-NH-}$ ,  $\text{-CH}_2\text{-C(O)-O-}$ ,  $\text{-CH}_2\text{-CH}_2\text{-C(O)-O-}$ , and  
 $\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-C(O)-O-}$ .

93. The polymeric reagent of claim 76, wherein the functional group is a ketone.

20 94. The polymeric reagent of claim 76, wherein the functional group is a ketone hydrate.

95. The polymeric reagent of claim 76, wherein the functional group is a hemiketal.

25 96. The polymeric reagent of claim 76, wherein the functional group is a ketal.

97. The polymeric reagent of claim 76, wherein the functional group is selected from the group consisting of thione, monothiohydrate, dithiohydrate, monothiohemiketal, dithiohemiketal, and dithioketal.

30 98. The polymeric reagent of claim 76, further comprising one or more additional water-soluble polymer segments.

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99. The polymeric reagent of claim 77, wherein (z) is a positive integer from 1 to 7, and each occurrence of R<sup>2</sup> and R<sup>3</sup> is H.

5 100. The polymeric reagent of claim 77, wherein (z) is a positive integer from 2 to 7.

101. The polymeric reagent of claim 77, wherein (z) is a positive integer from 1 to 7, and each of R<sup>2</sup> and R<sup>4</sup> attached to the carbon  $\alpha$  to FG-R<sup>14</sup> is alkyl, all other R<sup>2</sup> and R<sup>4</sup> are H, and each occurrence of R<sup>3</sup> and R<sup>5</sup> is H.

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102. The polymeric reagent of claim 77, wherein (b) is one, and EW<sup>1</sup> is selected from the group consisting of -O-, -NH-, -NHC(O)-, -C(O)NH-, -OC(O)-, -OC(O)-, -OC(O)-NH-, -NH-OC(O)-, -C(O)-, -C(S)-, and -C(OR)H-, wherein OR is an alkoxy or hydroxy substituent.

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103. The polymeric reagent of claim 77, wherein (a) is one and each of X<sup>1</sup> and X<sup>4</sup> is independently selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -O-C(O)-NH-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -C(O)-O-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-,

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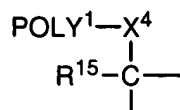
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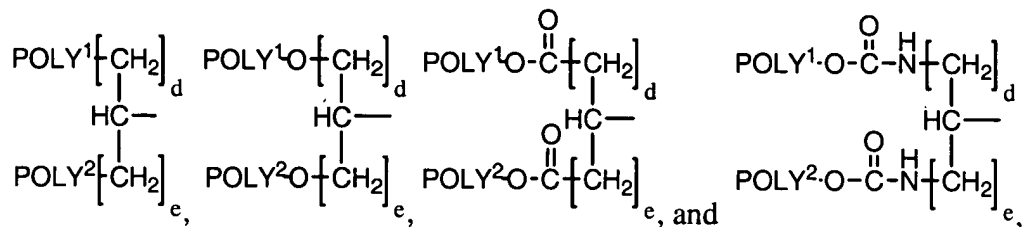
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 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-,  
 5 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -O-C(O)-NH-[CH<sub>2</sub>]<sub>0-6</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>0-2</sub>-, -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-,  
 -NH-C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-, -O-C(O)-CH<sub>2</sub>-, -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, and  
 -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, and X<sup>5</sup> is selected from the group consisting of -O-, -S-, -C(O)-,  
 -O-C(O)-, -C(O)-NH-, -NH-C(O)-NH-, -NH-C(O)-O-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-,  
 10 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-,  
 -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 15 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C(O)-,  
 -CH<sub>2</sub>-O-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-C(O)-, -CH<sub>2</sub>-C(O)-NH-,  
 20 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-,  
 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-C(O)-O-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-O-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-O-, -CH<sub>2</sub>-NH-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 25 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>0-6</sub>-NH-C(O)-O-, -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-,  
 30 -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-NH-, -CH<sub>2</sub>-C(O)-O-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-, and  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-.



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104. The polymeric reagent of claim 77, wherein  $\text{POLY}^2-\text{X}^5$ , is selected from the group consisting of:



wherein, in each instance:

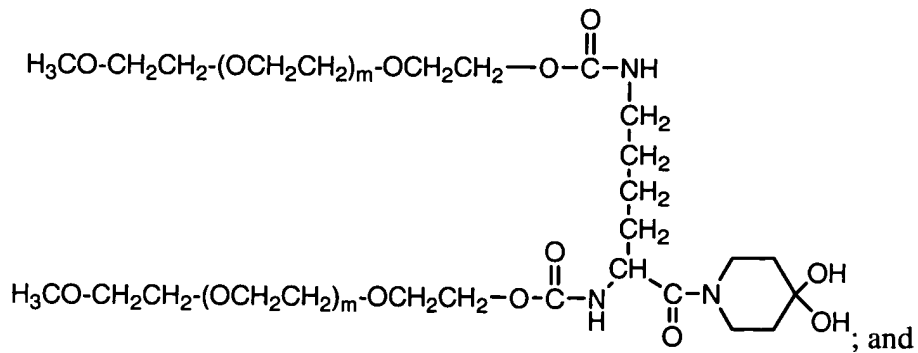
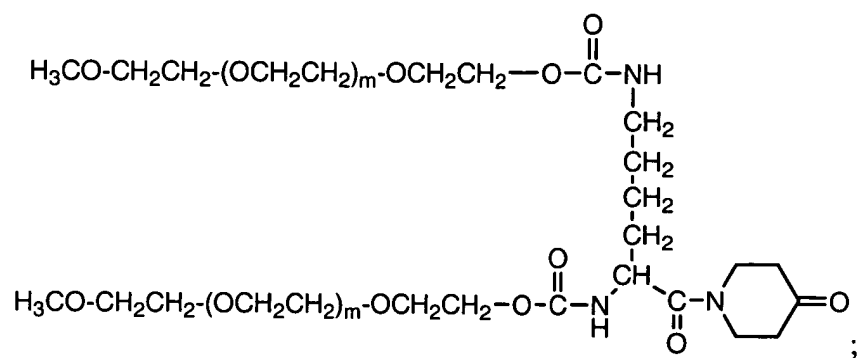
$\text{POLY}^1$ ,  $\text{POLY}^2$  is as previously defined;

(d) is 0 to 3; and

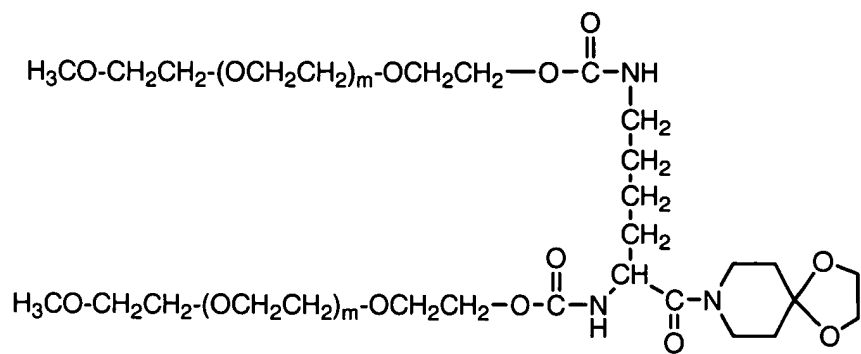
(e) is 0 to 3.

105. The polymeric reagent of claim 77, wherein  $\text{FG}-\text{R}^{14}$  is a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal having a terminus defined as  $\text{R}^1$ , wherein  $\text{R}^1$  is an organic radical selected from methyl and  $-\text{CH}=\text{CH}_2$ .

106. The polymeric reagent of claim 77, wherein  $\text{FG}-\text{R}^{14}$  is a cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure and further wherein the cyclic structure is selected from the group consisting of piperidiny, cyclohexyl, cyclopentyl, bicyclo[2,2,1]heptanyl, bicyclo[2,2,1]hexanyl, bicyclo[3,2,1]octanyl, bicyclo[3,1,1]heptanyl, bicyclo[3,3,1]nonanyl, cyclobutyl, cycloheptyl, cyclooctyl, oxa and aza forms thereof, and dioxo and diaza forms of any of the foregoing.



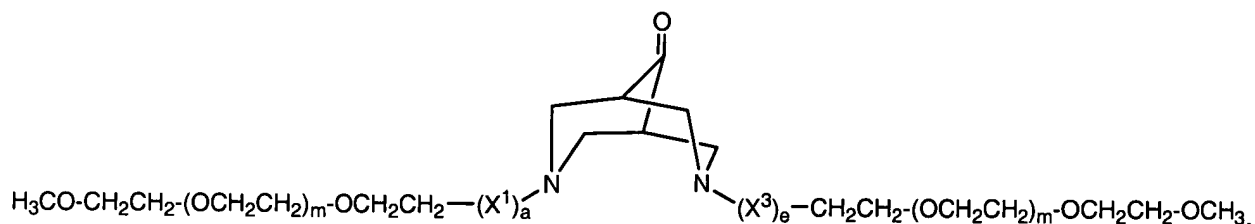
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wherein (m) is from about 25 to about 3000, and POLY<sup>1</sup>, POLY<sup>2</sup>, X<sup>4</sup> and X<sup>5</sup> are as previously defined.

108. The polymeric reagent of claim 77, further comprising one or more additional water-soluble polymer segments.

109. The polymeric reagent of claim 74, having the following structure:

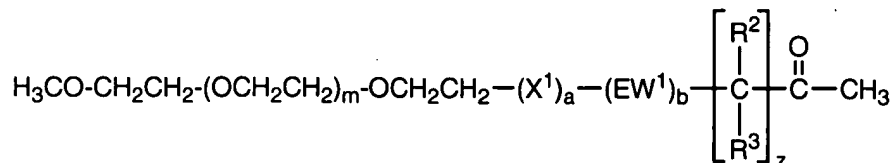


wherein (m) is from about 25 to about 3000, (a) is either zero or one, (e) is either zero or one, X<sup>1</sup> is a spacer moiety when present, and X<sup>3</sup> is a spacer moiety when present.

110. A polymeric reagent comprising a water-soluble polymer segment, wherein a functional group is attached to the water-soluble polymer segment through either a direct covalent bond or one or more atoms, and further wherein (a) the functional group is selected from the group consisting of thione, monothiohydrate, dithiohydrate, monothiohemiketal, dithiohemiketal, and dithiohemiketal, and (b) the polymeric reagent lacks a saturated hydrocarbon chain of 8 carbons or greater.

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111. A polymeric reagent composition comprising a polymeric reagent comprised of the following structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

$\text{X}^1$ , when present, is a spacer moiety;

$\text{EW}^1$ , when present, is an electron-withdrawing group;

(z) is from 1 to 8;

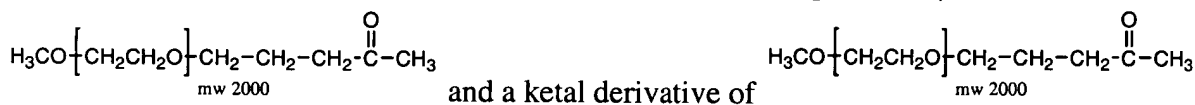
each occurrence of  $\text{R}^2$  is independently H or a nonaromatic-containing organic radical;

each occurrence of  $\text{R}^3$  is independently H or a nonaromatic-containing organic radical;

and

(m) is from 11 to about 3000,

wherein the composition is substantially free of oxidation side products,  $\beta$ -keto esters,



112. The composition of claim 111, wherein each occurrence of  $\text{R}^2$  and  $\text{R}^3$  is H.

113. The composition of claim 111, wherein the  $\text{R}^2$  attached to the carbon  $\alpha$  to the carbonyl carbon is alkyl, all other  $\text{R}^2$  are H, and each occurrence of  $\text{R}^3$  is H.

114. The composition of claim 111, wherein (a) is one and  $\text{X}^1$  is selected from the group consisting of -O-, -S-, -C(O)-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-NH-, -O-C(O)-NH-, -C(S)-, -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -O-CH<sub>2</sub>-, -CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O-, -C(O)-NH-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,

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-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-,  
 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-, -C(O)-O-CH<sub>2</sub>-,  
 5 -CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-O-CH<sub>2</sub>-, -C(O)-O-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-, -NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -C(O)-NH-CH<sub>2</sub>-,  
 -C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-, -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-,  
 -O-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-, -NH-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-NH-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-,  
 10 -C(O)-CH<sub>2</sub>-, -C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-C(O)-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-C(O)-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-,  
 -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-C(O)-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-,  
 15 -O-C(O)-NH-[CH<sub>2</sub>]<sub>0-6</sub>-(OCH<sub>2</sub>CH<sub>2</sub>)<sub>0-2</sub>-, -C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-,  
 -NH-C(O)-NH-(CH<sub>2</sub>)<sub>1-6</sub>-NH-C(O)-, -O-C(O)-CH<sub>2</sub>-, -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-, and  
 -O-C(O)-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-.

115. The composition of claim 111, wherein (b) is one and EW<sup>1</sup> is selected from the  
 20 group consisting of -NH-, -NHC(O)-, -C(O)NH-, -OC(O)-, -C(O)O-, -C(O)-, and -C(S)-.

116. The composition of claim 111, wherein (m) is from about 25 to about 3000.

117. The composition of claim 116, wherein (m) is from about 50 to about 3000.

118. The composition of claim 117, wherein (m) is from about 100 to about 3000.

119. The composition of claim 118, wherein (m) is from about 225 to about 3000.

120. The composition of claim 110, further comprising the ketone hydrate form of the  
 30 polymeric reagent.

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121. A method for making a polymeric reagent comprising the steps of:

(i) providing a precursor molecule comprised of at least one active anionic site suitable for initiating polymerization and a functional group or a protected form thereof, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal;

(ii) contacting the anionic site of the precursor molecule with a reactive monomer capable of polymerizing, to thereby initiate polymerization of the reactive monomer onto the precursor molecule;

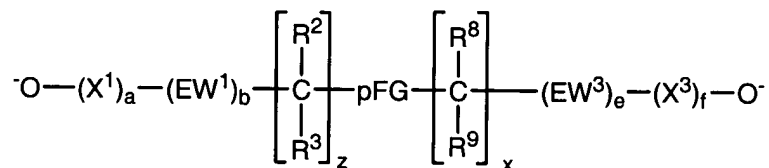
(iii) adding additional reactive monomers to the precursor molecule to form one or more polymer chains;

(iv) allowing said adding to continue until a desired length of the one or more polymer chains is reached;

(v) terminating the reaction, thereby resulting in a polymeric reagent comprised of the functional group or protected form thereof; and

(vi) optionally, when the functional group is in the protected form, deprotecting the functional group.

122. The method of claim 121, wherein the precursor molecule comprises the following structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

(e) is either zero or one;

(f) is either zero or one;

$\text{X}^1$ , when present, is a spacer moiety;

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$X^3$ , when present is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

$EW^3$ , when present, is an electron-withdrawing group;

(z) is zero or an integer from 1 to 8;

(x) is zero or an integer from 1 to 8;

when present, each  $R^2$  is independently H or an organic radical;

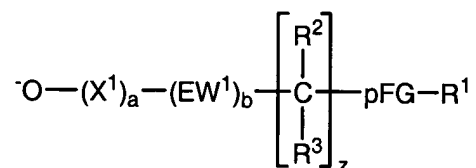
when present, each  $R^3$  is independently H or an organic radical;

when present, each  $R^8$  is independently H or an organic radical;

when present, each  $R^9$  is independently H or an organic radical; and

pFG is the functional group or a protected form thereof, wherein the functional group is selected from ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal.

123. The method of claim 121, wherein the precursor molecule comprises the following structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

$X^1$ , when present, is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

each occurrence of  $R^2$ , when present, is independently H or an organic radical;

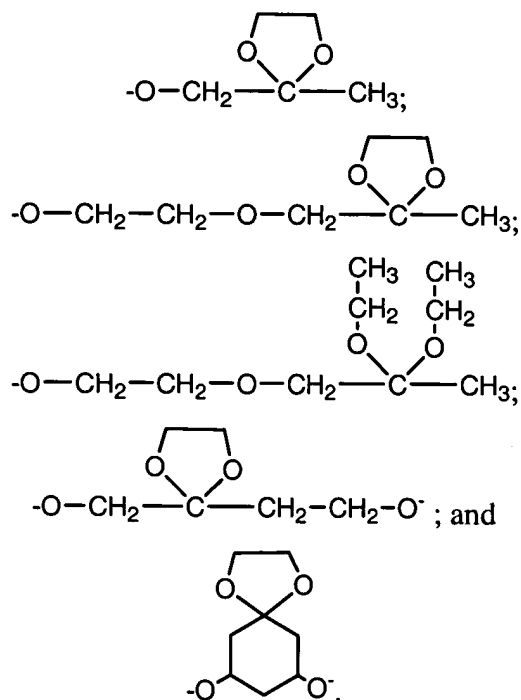
each occurrence of  $R^3$ , when present, is independently H or an organic radical; and

pFG- $R^1$  is either (i) a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal or a protected form of any of the foregoing, having a terminus defined as  $R^1$ , wherein  $R^1$  is an organic radical, or (ii) a cyclic structure wherein a

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functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure.

- 5           124. The method of claim 121, wherein the precursor molecule is selected from the group consisting of



125. The method of claim 121, wherein the reactive monomer is ethylene oxide.

- 15           126. The method of claim 121, further comprising the step of attaching an electrophilically reactive polymer to a terminal of the water-soluble polymer segment.

127. The method of claim 121, wherein the functional group is in protected form and the optional deprotecting step is performed.

- 20           128. A method for making a polymeric reagent comprising the steps of:

(i) providing a precursor molecule comprised of a protected secondary alcohol or thiol and at least one anionic site suitable for initiating polymerization;



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(ii) contacting the anionic site of the precursor molecule with a reactive monomer capable of polymerizing, to thereby initiate polymerization of the reactive monomer onto the precursor molecule;

(iii) adding additional reactive monomers to the precursor molecule to form one or more polymer chains;

(iv) allowing said contacting to continue until a desired length of the one or more polymer chains is reached;

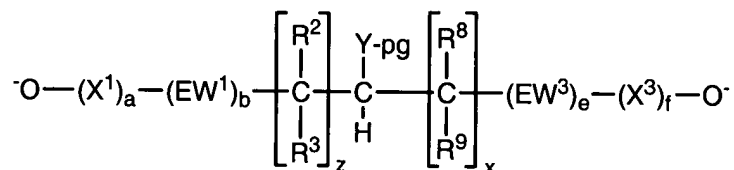
(v) terminating the reaction, thereby resulting in an intermediate comprised of the protected secondary alcohol or thiol;

(vi) deprotecting the protected secondary alcohol or thiol of the intermediate to form an unprotected secondary alcohol or thiol;

(vii) oxidizing the unprotected secondary alcohol or thiol to provide a polymeric reagent comprised of a ketone when the precursor molecule comprised a secondary alcohol or a thione when the precursor molecule comprised a secondary thiol; and

(viii) optionally further modifying the ketone or thione to result in a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal.

129. The method of claim 128, wherein the precursor molecule is comprised of the following structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

(e) is either zero or one;

(f) is either zero or one;

$\text{X}^1$ , when present, is a spacer moiety;

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$X^3$ , when present is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

$EW^3$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

5 (x) is zero or a positive integer from 1 to 7;

each occurrence of  $R^2$ , when present, is independently H or an organic radical;

each occurrence of  $R^3$ , when present, is independently H or an organic radical;

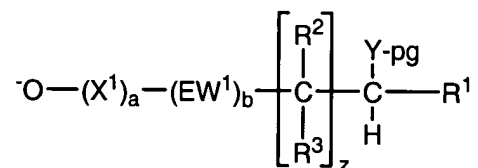
each occurrence of  $R^8$ , when present, is independently H or an organic radical;

each occurrence of  $R^9$ , when present, is independently H or an organic radical; and

10 Y is O or S; and

pg is a protecting group for a secondary alcohol when Y is O and a protecting group for a secondary thiol when Y is S.

15 130. The method of claim 128, wherein the precursor molecule is comprised of the following structure:



wherein:

20 (a) is either zero or one;

(b) is either zero or one;

$X^1$ , when present, is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

(z) is zero or an integer from 1 to 8;

25 each occurrence of  $R^2$ , when present, is independently H or an organic radical;

each occurrence of  $R^3$ , when present, is independently H or an organic radical;

Y is O or S;

pg is a protecting group for a secondary alcohol when Y is O and a protecting group for a secondary thiol when Y is S;

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and C-R<sup>1</sup> is either (i) a carbon atom having a terminus defined as R<sup>1</sup>, wherein R<sup>1</sup> is an organic radical, or (ii) a cyclic structure.

131. The method of claim 128, wherein the protected secondary alcohol or thiol is protected through a protecting group selected from the group consisting of benzyl ether, methoxymethyl ether (MOM), methylthiomethyl ether (MTM), tetrahydropyranyl ether (THP), 4-methoxytetrahydropyranyl ether, tetrahydrofuranyl ether, 1-ethoxyethyl ether, 1-methyl-1-methoxyethyl ether, 2-(phenylselenyl)ethyl ether, allyl ether, *o*-nitrobenzyl ether, triphenylmethyl ether,  $\alpha$ -naphthyldiphenylmethyl ether, *p*-methoxyphenyldiphenylmethyl ether, 9-(9-phenyl-10-oxo)anthryl ether (tritylone), isopropyldimethylsilyl ether, *t*-butyldimethylsilyl ether (TBDMS), tribenzylsilyl ether, and triisopropylsilyl ether.

132. The method of claim 131, wherein the protecting group is benzyl ether.

133. The method of claim 128, wherein the reactive monomer is ethylene oxide.

134. The method of claim 128, further comprising the step of attaching an electrophilically reactive polymer to a terminal of the water-soluble polymer segment.

135. The method of claim 128, wherein the deprotecting step is carried out under in the presence of H<sub>2</sub> and a metal.

136. The method of claim 135, wherein the metal is nickel, platinum, or lead.

137. The method of claim 128, wherein the oxidizing step is carried under oxidizing conditions comprised of a reagent selected from the group consisting of KMnO<sub>4</sub>, MnO<sub>2</sub>, K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, CrO<sub>3</sub>, pyridinium chlorochromate, pyridinium fluorochromate, pyridinium dichromate, RuO<sub>4</sub>, RuCl<sub>3</sub>, tetra-*n*-propylammonium perruthenate, dimethyl sulfoxide, *N*-chlorosuccinimide, Ag<sub>2</sub>CO<sub>3</sub>, Ag<sub>2</sub>O, and Dess-Martin periodinane reagents.

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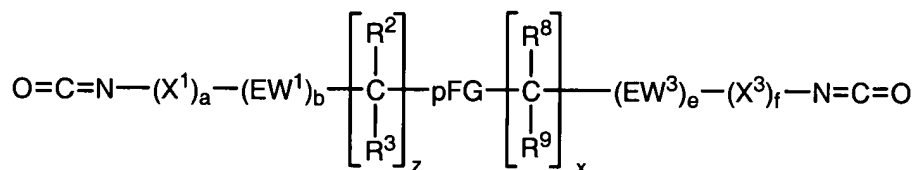
138. A method for making a polymeric reagent comprising the steps of:

(i) providing an precursor molecule comprised of at least one isocyanate moiety and a functional group or a protected form thereof, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal; and

(ii) contacting, under suitable reaction conditions, the precursor molecule and a water-soluble polymer segment bearing at least one hydroxyl group or amine group to thereby form a polymeric reagent comprising the functional group or protected form thereof; and

(iii) optionally, when the functional group is in the protected form, deprotecting the functional group.

139. The method of claim 138, wherein the precursor molecule comprises the following structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

(e) is either zero or one;

(f) is either zero or one;

$\text{X}^1$ , when present, is a spacer moiety;

$\text{X}^3$ , when present is a spacer moiety;

$\text{EW}^1$ , when present, is an electron-withdrawing group;

$\text{EW}^3$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

(x) is zero or a positive integer from 1 to 7;

each occurrence of  $\text{R}^2$ , when present, is independently H or an organic radical;

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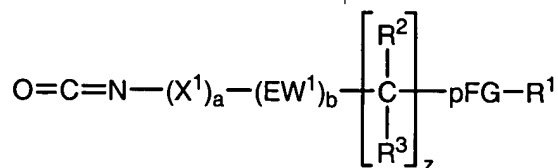
each occurrence of  $R^3$ , when present, is independently H or an organic radical;

each occurrence of  $R^8$ , when present, is independently H or an organic radical;

each occurrence of  $R^9$ , when present, is independently H or an organic radical; and

pFG is the functional group or a protected form thereof, wherein the functional group is  
 5 selected from ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal.

140. The method of claim 138, wherein the precursor molecule comprises the following  
 structure:



wherein:

(a) is either zero or one;

(b) is either zero or one;

$X^1$ , when present, is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

each occurrence of  $R^2$ , when present, is independently H or an organic radical;

each occurrence of  $R^3$ , when present, is independently H or an organic radical; and

pFG- $R^1$  is either (i) a functional group selected from the group consisting of ketone,  
 ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal,  
 dithiohemiketal, ketal, and dithioketal or a protected form of any of the foregoing, having a  
 terminus defined as  $R^1$ , wherein  $R^1$  is an organic radical, or (ii) a cyclic structure wherein a  
 functional group selected from the group consisting of ketone, ketone hydrate, thione,  
 monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and  
 dithioketal is part of the cyclic structure.

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141. The method of claim 140, wherein the water-soluble polymer segment has only one terminal hydroxyl group thereby providing a polymeric reagent with a single functional group or protected form thereof.

5           142. The method of claim 140, wherein the water-soluble polymer segment has two terminal hydroxy groups, thereby providing a polymeric reagent with two functional groups or protected forms thereof.

10           143. The method of claim 138, wherein the functional group is in protected form and the optional deprotecting step is performed.

144. A method for making a polymeric reagent comprising the steps of:

(i) providing a water-soluble polymer segment having at least one available nucleophilic group;

15           (ii) providing a precursor molecule comprised of at least one activating group and a functional group or a protected form thereof, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal;

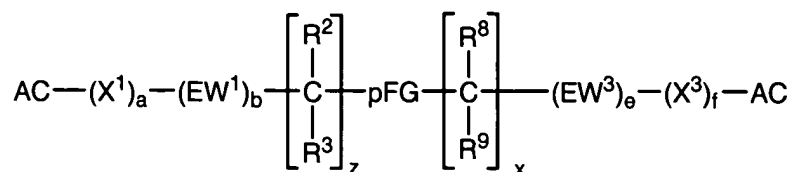
20           (iii) contacting, under suitable reaction conditions, the precursor molecule with the water-soluble polymer segment, thereby forming a polymeric reagent comprising the functional group or protected form thereof; and

(iv) optionally, when the functional group is in the protected form, deprotecting the functional group.

25           145. The method of claim 144, wherein the water-soluble polymer segment having at least one available nucleophilic group is an amine-terminated poly(ethylene glycol).

146. The method of claim 144, wherein the precursor molecule comprises the following structure:

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wherein:

(a) is either zero or one;

(b) is either zero or one;

5 (e) is either zero or one;

(f) is either zero or one;

$\text{X}^1$ , when present, is a spacer moiety;

$\text{X}^3$ , when present is a spacer moiety;

$\text{EW}^1$ , when present, is an electron-withdrawing group;

10  $\text{EW}^3$ , when present, is an electron-withdrawing group;

(z) is zero or a positive integer from 1 to 7;

(x) is zero or a positive integer from 1 to 7;

each occurrence of  $\text{R}^2$ , when present, is independently H or an organic radical;

each occurrence of  $\text{R}^3$ , when present, is independently H or an organic radical;

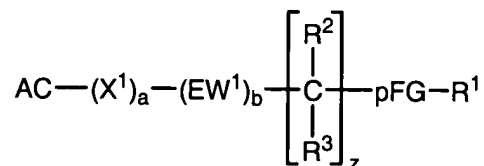
15 each occurrence of  $\text{R}^8$ , when present, is independently H or an organic radical;

each occurrence of  $\text{R}^9$ , when present, is independently H or an organic radical;

pFG is the functional group or a protected form thereof, wherein the functional group is ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal; and

20 each AC is an activating group.

147. The method of claim 144, wherein the precursor molecule comprises the following structure:



25

wherein:

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(a) is either zero or one;

(b) is either zero or one;

$X^1$ , when present, is a spacer moiety;

$EW^1$ , when present, is an electron-withdrawing group;

(z) is zero or an integer from 1 to 8;

each occurrence of  $R^2$ , when present, is independently H or an organic radical;

each occurrence of  $R^3$ , when present, is independently H or an organic radical; and

$pFG-R^1$  is either (i) a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal or a protected form of any of the foregoing, having a terminus defined as  $R^1$ , wherein  $R^1$  is an organic radical, or (ii) a cyclic structure wherein a functional group selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal is part of the cyclic structure; and

AC is an activating group.

148. The method of claim 147, wherein the water-soluble polymer segment has only one terminal amine group thereby providing a polymeric reagent with a single functional group or protected form thereof.

149. The method of claim 147, wherein the water-soluble polymer segment has two terminal amine groups, thereby providing a polymeric reagent with two functional groups or protected forms thereof.

150. The method of claim 144, wherein the functional group is in protected form and the optional deprotecting step is performed.

151. A method for making a polymeric reagent comprising the steps of:

(i) providing a water-soluble polymer segment having at least one available leaving group;



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(ii) providing a precursor molecule comprised of at least one nucleophilic group and a functional group or a protected form thereof, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal;

5 (iii) contacting, under suitable reaction conditions, the precursor molecule with the water-soluble polymer segment, thereby forming a polymeric reagent comprising the functional group or protected form thereof; and

(iv) optionally, when the functional group is in the protected form, deprotecting the functional group.

10 152. The method of claim 151, wherein the leaving group is a primary halogen or a secondary halogen.

153. The method of claim 151, wherein the leaving group is a sulfonate ester.

15 154. The method of claim 153, wherein the sulfonate ester is selected from the group consisting of methanesulfonate, trifluoromethanesulfonate, trichloromethanesulfonate, 2,2,2-trifluoroethanesulfonate, 2,2,2-trichloroethanesulfonate, nonafluorobutanesulfonate, para-bromobenzenesulfonate, para-nitrobenzenesulfonate, and para-toluenesulfonate.

20 155. The method of claim 151, wherein the functional group is in protected form and the optional deprotecting step is performed.

25 156. A method for making a polymeric reagent comprising the step of reacting a water-soluble polymer segment having at least one alkoxide ion or thiolate ion with precursor molecule comprised of at least one leaving group and a functional group or a protected form thereof, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal, dithiohemiketal, ketal, and dithioketal, thereby providing a polymeric reagent.

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157. The method of claim 156, wherein the water-soluble polymer segment having at least one alkoxide ion or thiolate ion is prepared by combining a water-soluble polymer having at least one hydroxyl group in the presence of a suitable base.

5

158. The method of claim 157, wherein the suitable base is selected from the group consisting of sodium, sodium hydroxide, potassium, potassium hydroxide, sodium hydride, potassium hydride, sodium methoxide, potassium methoxide, sodium tert-butoxide, potassium tert-butoxide, sodium carbonate, and potassium carbonate.

10

159. The method of claim 156, wherein the water-soluble polymer segment having at least one alkoxide ion or thiolate ion is provided via a polymerization reaction.

15

160. A polymer-active agent conjugate comprising a covalent bond between a nitrogen atom of an active agent to a secondary carbon atom, wherein the secondary carbon atom is attached, either directly or through one or more atoms, to a water-soluble polymer segment

20

161. The conjugate of claim 160, wherein the conjugate lacks a hydroxyl moiety attached to the secondary carbon atom.

162. The conjugate of claim 160, wherein the conjugate lacks a carbonyl moiety attached to a carbon atom adjacent to the secondary carbon atom.

25

163. The conjugate of claim 160, wherein the conjugate lacks both (a) a hydroxyl moiety attached to the secondary carbon atom, and (b) a carbonyl moiety attached to a carbon atom adjacent to the secondary carbon atom.

164. The conjugate of claim 160, wherein a methyl group is attached to a carbon adjacent to the secondary carbon atom.

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165. The conjugate of claim 160, wherein the water-soluble polymer segment is branched.

5           166. The conjugate of claim 160, comprising a second water-soluble polymer segment attached, either directly or through one or more atoms, to the secondary carbon atom.

167. The conjugate of claim 160, wherein the active agent is a polypeptide.

10           168. The conjugate of claim 160, wherein the active agent is not a polypeptide.

169. A pharmaceutical preparation comprising the conjugate of claim 160 and a pharmaceutically acceptable excipient.

15           170. A method for making a polymer-active agent conjugate comprising contacting, under conjugation conditions, an active agent with a polymeric reagent comprised of a water-soluble polymer segment attached, either directly or through one or more atoms, to a functional group, wherein the functional group is selected from the group consisting of ketone, ketone hydrate, thione, monothiohydrate, dithiohydrate, hemiketal, monothiohemiketal,  
20           dithiohemiketal, ketal, and dithioketal.

171. The method of claim 170, wherein the polymeric reagent is encompassed by one of claims 1, 14, 35, 54, 75, or 110.

25           172. The method of claim 171, wherein the functional group is a ketone.

173. The method of claim 171, wherein the functional group is a ketone hydrate.

174. The method of claim 171, wherein the functional group is a hemiketal.

30

175. The method of claim 171, wherein the functional group is a ketal.

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176. The method of claim 171, wherein the functional group is a thione.

177. The method of claim 171, wherein the functional group is a monothiohydrate.

178. The method of claim 171, wherein the functional group is a dithiohydrate.

179. The method of claim 171, wherein the functional group is a monothiohemiketal,

180. The method of claim 171, wherein the functional group is a dithiohemiketal.

181. The method of claim 171, wherein the functional group is a dithioketal.

182. The method of claim 171, wherein the active agent is a polypeptide.

183. The method of claim 171, wherein the active agent is a polypeptide.

184. The method of claim 171, wherein the active agent is not a polypeptide.

185. A polymeric reagent prepared in accordance with any one of claims 121, 128, 138, 144, 151, or 156.

186. A polymer-active agent conjugate prepared from contacting an active agent with a polymeric reagent encompassed by any one of claims 1, 14, 35, 54, 75, or 110.